

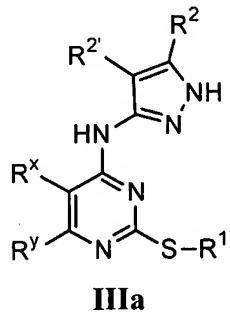
any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-0740.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in this paper or documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to Deposit Account No. 50-0740.

AMENDMENTS TO THE CLAIMS

Please cancel claims 12-14 without prejudice to or disclaimer of the subject matter recited therein. Please add new claim 30.

1. (Previously presented) A compound of formula **IIIa**:



or a pharmaceutically acceptable salt thereof, wherein:

R^x and R^y are independently selected from T-R³ or L-Z-R³;

R¹ is T-(Ring D);

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon

of Ring D is independently substituted by oxo, T-R⁵, or V-Z-R⁵, and each substitutable ring nitrogen of Ring D is independently substituted by -R⁴;

T is a valence bond or a C₁₋₄ alkylidene chain;

Z is a C₁₋₄ alkylidene chain;

L is -O-, -S-, -SO-, -SO₂-, -N(R⁶)SO₂-, -SO₂N(R⁶)-, -N(R⁶)-, -CO-, -CO₂-, -N(R⁶)CO-, -N(R⁶)C(O)O-, -N(R⁶)CON(R⁶)-, -N(R⁶)SO₂N(R⁶)-, -N(R⁶)N(R⁶)-, -C(O)N(R⁶)-, -OC(O)N(R⁶)-, -C(R⁶)₂O-, -C(R⁶)₂S-, -C(R⁶)₂SO-, -C(R⁶)₂SO₂-, -C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-, -C(R⁶)₂N(R⁶)C(O)-, -C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-, -C(R⁶)=N-O-, -C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-, or -C(R⁶)₂N(R⁶)CON(R⁶)-;

R² and R^{2'} are independently selected from -R, -T-W-R⁶, or R² and R^{2'} are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R² and R^{2'} is independently substituted by halo, oxo, -CN, -NO₂, -R⁷, or -V-R⁶, and each substitutable ring nitrogen of said ring formed by R² and R^{2'} is independently substituted by R⁴;

R³ is selected from -R, -halo, -OR, -C(=O)R, -CO₂R, -COCOR, -COCH₂COR, -NO₂, -CN, -S(O)R, -S(O)₂R, -SR, -N(R⁴)₂, -CON(R⁷)₂, -SO₂N(R⁷)₂, -OC(=O)R, -N(R⁷)COR, -N(R⁷)CO₂(C₁₋₆ aliphatic), -N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁷)CON(R⁷)₂, -N(R⁷)SO₂N(R⁷)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁷)₂;

each R is independently selected from hydrogen or an optionally substituted group selected from C₁₋₆ aliphatic, C₆₋₁₀ aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R⁴ is independently selected from -R⁷, -COR⁷, -CO₂(optionally substituted C₁₋₆ aliphatic), -CON(R⁷)₂, or -SO₂R⁷;

each R⁵ is independently selected from -R, halo, -OR, -C(=O)R, -CO₂R, -COCOR, -NO₂, -CN, -S(O)R, -SO₂R, -SR, -N(R⁴)₂, -CON(R⁴)₂, -SO₂N(R⁴)₂, -OC(=O)R, -N(R⁴)COR, -N(R⁴)CO₂(optionally substituted C₁₋₆ aliphatic), -N(R⁴)N(R⁴)₂, -C=NN(R⁴)₂, -C=N-OR, -N(R⁴)CON(R⁴)₂, -N(R⁴)SO₂N(R⁴)₂, -N(R⁴)SO₂R, or -OC(=O)N(R⁴)₂;

V is -O-, -S-, -SO-, -SO₂-, -N(R⁶)SO₂-, -SO₂N(R⁶)-, -N(R⁶)-, -CO-, -CO₂-, -N(R⁶)CO-,

-N(R⁶)C(O)O-, -N(R⁶)CON(R⁶)-, -N(R⁶)SO₂N(R⁶)-, -N(R⁶)N(R⁶)-, -C(O)N(R⁶)-, -OC(O)N(R⁶)-, -C(R⁶)₂O-, -C(R⁶)₂S-, -C(R⁶)₂SO-, -C(R⁶)₂SO₂-, -C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-, -C(R⁶)₂N(R⁶)C(O)-, -C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-, -C(R⁶)=N-O-, -C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-, or -C(R⁶)₂N(R⁶)CON(R⁶)-;

W is -C(R⁶)₂O-, -C(R⁶)₂S-, -C(R⁶)₂SO-, -C(R⁶)₂SO₂-, -C(R⁶)₂SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)-, -CO-, -CO₂-, -C(R⁶)OC(O)-, -C(R⁶)OC(O)N(R⁶)-, -C(R⁶)₂N(R⁶)CO-, -C(R⁶)₂N(R⁶)C(O)O-, -C(R⁶)=NN(R⁶)-, -C(R⁶)=N-O-, -C(R⁶)₂N(R⁶)N(R⁶)-, -C(R⁶)₂N(R⁶)SO₂N(R⁶)-, -C(R⁶)₂N(R⁶)CON(R⁶)-, or -CON(R⁶)-;

each R⁶ is independently selected from hydrogen or an optionally substituted C₁₋₄ aliphatic group, or two R⁶ groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring; and

each R⁷ is independently selected from hydrogen or an optionally substituted C₁₋₆ aliphatic group, or two R⁷ on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring,

wherein optional substituents of C₆₋₁₀ aryl and optional substituents of a heteroaryl ring having 5-10 ring atoms are selected from: a halogen, -R°, -OR°, -SR°, 1,2-methylene-dioxy, 1,2-ethylenedioxy, protected OH, phenyl (Ph), substituted Ph, -O(Ph), substituted -O(Ph), -CH₂(Ph), substituted -CH₂(Ph), -CH₂CH₂(Ph), substituted -CH₂CH₂(Ph), -NO₂, -CN, -N(R°)₂, -NR°C(O)R°, -NR°C(O)N(R°)₂, -NR°CO₂R°, -NR°NR°C(O)R°, -NR°NR°C(O)N(R°)₂, -NR°NR°CO₂R°, -C(O)C(O)R°, -C(O)CH₂C(O)R°, -CO₂R°, -C(O)R°, -C(O)N(R°)₂, -OC(O)N(R°)₂, -S(O)₂R°, -SO₂N(R°)₂, -S(O)R°, -NR°SO₂N(R°)₂, -NR°SO₂R°, -C(=S)N(R°)₂, -C(=NH)-N(R°)₂, -(CH₂)_yNHC(O)R°, or -(CH₂)_yNHC(O)CH(V'-R°)(R°), wherein each R° is independently selected from hydrogen, a substituted or unsubstituted aliphatic group, an unsubstituted heteroaryl or heterocyclic ring, phenyl (Ph), substituted Ph, -O(Ph), substituted -O(Ph), -CH₂(Ph), and substituted -CH₂(Ph), wherein y' is 0-6, wherein V' is a linker group, and wherein substituents on the aliphatic group or the phenyl ring of R° are selected from amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyl,

alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alkoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, and haloalkyl; wherein optional substituents of C₁₋₆ aliphatic are selected from: the optional substituents of the C₆₋₁₀ aryl, the optional substituents of the heteroaryl ring, =O, =S, =NNHR^{*}, =NN(R^{*})₂, =N-, =NNHC(O)R^{*}, =NNHCO₂(alkyl), =NNHSO₂(alkyl), and =NR^{*}, wherein each R^{*} is independently selected from hydrogen, an unsubstituted aliphatic group, and a substituted aliphatic group, and wherein substituents on the aliphatic group are selected from amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alkoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, and haloalkyl; and wherein optional substituents of a heterocyclyl ring having 5-10 ring atoms are selected from: -R⁺, -N(R⁺)₂, -C(O)R⁺, -CO₂R⁺, -C(O)C(O)R⁺, -C(O)CH₂C(O)R⁺, -SO₂R⁺, -SO₂N(R⁺)₂, -C(=S)N(R⁺)₂, -C(=NH)-N(R⁺)₂, and -NR⁺SO₂R⁺, wherein each R⁺ is independently selected from hydrogen, an aliphatic group, a substituted aliphatic group, phenyl (Ph), substituted Ph, -O(Ph), substituted -O(Ph), CH₂(Ph), substituted CH₂(Ph), and an unsubstituted heteroaryl or heterocyclic ring, wherein substituents on the aliphatic group or the phenyl ring are selected from amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alkoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, and haloalkyl.

2. (Previously presented) The compound according to claim 1, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C₁₋₄ aliphatic group;
- (b) R^y is T-R³ or L-Z-R³, wherein T is a valence bond or a methylene and R³ is -R, -N(R⁴)₂, or -OR;
- (c) R¹ is T-(Ring D), wherein T is a valence bond or a methylene unit;
- (d) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (e) R² is -R or -T-W-R⁶ and R^{2'} is hydrogen, or R² and R^{2'} are taken together to form a benzo ring, wherein the benzo ring is optionally substituted with a group selected

from -halo, -N(R⁴)₂, -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, -NO₂, -O(C₁₋₄ alkyl), -CO₂(C₁₋₄ alkyl), -CN, -SO₂(C₁₋₄ alkyl), -SO₂NH₂, -OC(O)NH₂, -NH₂SO₂(C₁₋₄ alkyl), -NHC(O)(C₁₋₄ alkyl), -C(O)NH₂, and -CO(C₁₋₄ alkyl), wherein the (C₁₋₄ alkyl) is a straight, branched, or cyclic alkyl group.

3. (Original) The compound according to claim 2, wherein:

- (a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C₁₋₄ aliphatic group;
- (b) R^y is T-R³ or L-Z-R³, wherein T is a valence bond or a methylene and R³ is -R, -N(R⁴)₂, or -OR;
- (c) R¹ is T-(Ring D), wherein T is a valence bond or a methylene unit;
- (d) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and
- (e) R² is -R or -T-W-R⁶ and R^{2'} is hydrogen, or R² and R^{2'} are taken together to form an optionally substituted benzo ring.

4. (Original) The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

- (a) R^y is T-R³ or L-Z-R³ wherein T is a valence bond or a methylene and R³ is selected from -R, -OR, or -N(R⁴)₂, wherein R is selected from hydrogen, C₁₋₆ aliphatic, or 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl;
- (b) R¹ is T-(Ring D), wherein T is a valence bond;
- (c) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring;
- (d) R² is -R and R^{2'} is hydrogen, wherein R is selected from hydrogen, C₁₋₆ aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring; and
- (e) L is -O-, -S-, or -N(R⁴)-.

5. (Original) The compound according to claim 4, wherein:

- (a) R^y is $T-R^3$ or $L-Z-R^3$ wherein T is a valence bond or a methylene and R^3 is selected from $-R$, $-OR$, or $-N(R^4)_2$, wherein R is selected from hydrogen, C₁₋₆ aliphatic, or 5-6 membered heterocyclyl, phenyl, or 5-6 membered heteroaryl;
- (b) R^1 is $T-(Ring\ D)$, wherein T is a valence bond;
- (c) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring;
- (d) R^2 is $-R$ and R^2 is hydrogen, wherein R is selected from hydrogen, C₁₋₆ aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring; and
- (e) L is $-O-$, $-S-$, or $-N(R^4)-$.

6. (Previously presented) The compound according to claim 4, wherein said compound has one or more features selected from the group consisting of:

- (a) R^x is hydrogen, methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetimido;
- (b) R^y is selected from 2-pyridyl, 4-pyridyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, methyl, ethyl, cyclopropyl, isopropyl, t-butyl, alkoxyalkylamino, alkoxyalkyl, alkyl- or dialkylamino, alkyl- or dialkylaminoalkoxy, acetamido, optionally substituted phenyl, or methoxymethyl;
- (c) R^1 is $T-(Ring\ D)$, wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, $-N(R^4)_2$, optionally substituted C₁₋₆ aliphatic group, -OR, -CO₂R, -CONH(R⁴), $-N(R^4)COR$, $-N(R^4)SO_2R$, $-N(R^6)COCH_2CH_2N(R^4)_2$, or $-N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and
- (d) R^2 is hydrogen or a substituted or unsubstituted C₁₋₆ aliphatic, and L is $-O-$, $-S-$, or $-NH-$.

7. (Previously presented) The compound according to claim 6, wherein:

- (a) R^x is hydrogen, methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetimido;

- (b) R^y is selected from 2-pyridyl, 4-pyridyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, methyl, ethyl, cyclopropyl, isopropyl, t-butyl, alkoxyalkylamino, alkoxyalkyl, alkyl- or dialkylamino, alkyl- or dialkylaminoalkoxy, acetamido, optionally substituted phenyl, or methoxymethyl;
- (c) R¹ is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO₂, -N(R⁴)₂, optionally substituted C₁₋₆ aliphatic group, -OR, -CO₂R, -CONH(R⁴), -N(R⁴)COR, -N(R⁴)SO₂R, -N(R⁶)COCH₂CH₂N(R⁴)₂, or -N(R⁶)COCH₂CH₂CH₂N(R⁴)₂; and
- (d) R² is hydrogen or a substituted or unsubstituted C₁₋₆ aliphatic, and L is -O-, -S-, or -NH-.

8. (Canceled)

9. (Previously presented) A composition comprising a compound according to any one of claims 1-7, and a pharmaceutically acceptable carrier.

10. (Original) The composition according to claim 9, further comprising an additional therapeutic agent.

11. (Canceled)

12. (Canceled)

13. (Canceled)

14. (Canceled)

15. (Previously presented) A method of treating an Aurora-2-mediated disease selected from colon, breast, stomach, or ovarian cancer, which method comprises administering to a

patient in need of such a treatment a therapeutically effective amount of a composition according to claim 9.

16. (Canceled)

17. (Previously presented) The method according to claim 15, wherein said method further comprises administering an additional therapeutic agent.

18. (Original) The method according to claim 17, wherein said additional therapeutic agent is a chemotherapeutic agent.

19. (Previously presented) A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 9, wherein the patient is in need of treatment of a disease selected from diabetes, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), or cardiomyocyte hypertrophy.

20. (Previously presented) A method of inhibiting GSK-3 activity in a patient comprising the step of administering to said patient a composition according to claim 10, wherein the patient is in need of treatment of a disease selected from diabetes, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), or cardiomyocyte hypertrophy.

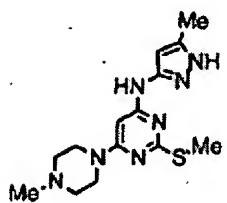
21. (Previously presented) A method of treating a GSK-3-mediated disease selected from diabetes, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), or cardiomyocyte hypertrophy, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 9.

22. (Canceled)

23. (Original) The method according to claim 21, wherein said GSK-3-mediated disease is diabetes.

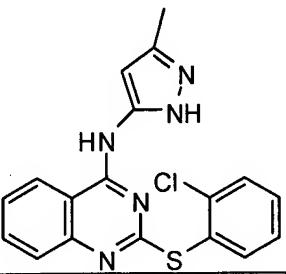
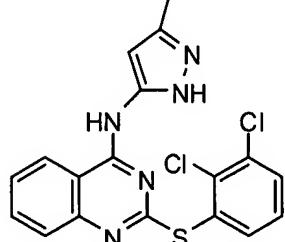
Claims 24 - 28. (Canceled)

Claim 29. (Previously presented) The compound IIIa-14:



Claim 30. (New) A compound selected from the the following formula IIa compounds, or a pharmaceutically acceptable salt thereof:

IIa-1	<p>Chemical structure of compound IIa-1: A 2-phenylthio-4-(2-methylimidazol-2-yl)imidazole derivative. It consists of a 2-phenylthioimidazole ring fused to a 2-methylimidazole ring. The 4-position of the imidazole ring is substituted with a 2-phenylthio group.</p>	IIa-2	<p>Chemical structure of compound IIa-2: A 2-chlorophenylthio-4-(2-methylimidazol-2-yl)imidazole derivative. It consists of a 2-chlorophenylthioimidazole ring fused to a 2-methylimidazole ring. The 4-position of the imidazole ring is substituted with a 2-chlorophenylthio group.</p>
IIa-3	<p>Chemical structure of compound IIa-3: A 2,4-dichlorophenylthio-4-(2-methylimidazol-2-yl)imidazole derivative. It consists of a 2,4-dichlorophenylthioimidazole ring fused to a 2-methylimidazole ring. The 4-position of the imidazole ring is substituted with a 2,4-dichlorophenylthio group.</p>	IIa-5	<p>Chemical structure of compound IIa-5: A 2-ethylphenylthio-4-(2-methylimidazol-2-yl)imidazole derivative. It consists of a 2-ethylphenylthioimidazole ring fused to a 2-methylimidazole ring. The 4-position of the imidazole ring is substituted with a 2-ethylphenylthio group.</p>

IIa-7		IIa-8	
IIa-9	